

### **REMARKS**

Claims 14-17 and 25-29 are currently pending in the application. By this amendment, claims 16, 17 and 25 are amended and new claims 26-29 are added for the Examiner's consideration. The foregoing separate sheets marked as "Listing of Claims" show all the claims in the application, with an indication of the current status of each.

#### **Claim Rejections 35 U.S.C. 112(b)**

Claims 14-17 and 25 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards, as the invention. Examiner states that the recitation of "or tissue precursor" is unclear.

Claim 25 has hereby been amended by deleting the phrase "or tissue precursor", thereby making moot this rejection.

In view of the foregoing, reconsideration and withdrawal of this rejection is requested.

#### **Claim Rejections: 35 USC § 102(b)**

Claims 14, 15 and 25 stand rejected under 35 USC § 102(b) as anticipated by Vacanti et al., (US 5,770,417, hereafter "Vacanti"). This rejection is traversed.

Vacanti describes a method of producing functional organ equivalents using bioabsorbable artificial substrates as temporary scaffolding for cellular transfer and implantation (column 5, lines 20-22). In the method, cells are initially cultured on a scaffolding using known techniques until they have begun to grow and cover the matrix. They are then implanted *in vivo* at a site appropriate for attachment, growth and function, and for vascularization to occur (column 6, line 9-12). In other words, vascularization of the structure occurs *in vivo* after implantation (column 6, lines 16-17). Vacanti's device, at the time of implantation, has no vascularization as is required in the claimed invention.

In fact, one object of the invention of Vacanti is to provide support matrices that are configured with sufficient surface area so as to allow sufficient diffusion of nutrients and waste products both *in vitro* and *in vivo* "prior to the ingrowth of blood vessels following implantation" (see column 5, lines 38-46, emphasis added). Vacanti recognizes that the need for sufficient

diffusion is crucial, suggesting that the maximum diffusion distance is 2-3 mm, and that scaffolds must be constructed accordingly to allow diffusion “until new blood vessels form.” (Column 5, lines 35-36). In other words, Vacanti recognizes the need to design the support matrices in a manner that allows sufficient diffusion of nutrients and waste products both *in vitro* and *in vivo* because, according to the method of Vacanti, vascularization does not occur during cultivation *in vitro*, and *in vivo* vascularization occurs only after some (unspecified) time post-implantation.

In contrast, the present invention address the problem of supplying nutrients and eliminating waste products in bioartificially grown tissues in another manner. According to the method of the present invention, the cells that are growing on an artificial scaffolding are supplied with at least one vessel and, as a result, develop vasculature while they are cultured *in vitro*, before being implanted. Thus, vasculaturization of the tissue occurs during the course of cultivation of the bioartificial tissue and is already present by the time the bioartificial construct, according to the claimed invention, is implanted into a recipient. This concept is described, for example, on page 5 at lines 5-9, and on page 5, at lines 10-25, details of the type of vessel and its preferred characteristics are described. Claim 25 thus recites a vascularized bioartificial tissue made by the process of inserting at least one vascularizing vessel into a mixture of viable cells in or on a matrix whereby the at least one vessel is inserted prior to or at the beginning of cultivation of the mixture of the matrix and cells; and cultivating said mixture, wherein the at least one vessel propagates and a vascularized bioartificial tissue is obtained, and wherein the step of cultivating includes supplying constituents to said at least one vessel from a location remote from said tissue.

Clearly, Vacanti does not anticipate the subject matter of claim 25, since Vacanti does not provide bioartificial tissue that is vascularized prior to or at the beginning of cultivation by insertion of at least one vessel, as is required by claim 25. Vacanti does not provide vascularized bioartificial tissue at all.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of this rejection.

#### **Claim Rejections: 35 USC § 103(a)**

Claims 16 and 17 of the present application stand rejected under 35 USC § 103(a) as obvious over Vacanti. This rejection is traversed.

As described above, the bioartificial tissue described by Vacanti is fundamentally different from that of the present invention, the characteristics of which are recited in independent claim 25. The bioartificial tissue of Vacanti is not vascularized prior to implantation, whereas that of the present invention is due to provision of a vascularizing vessel before or at the time of initial cultivation of cells and a support matrix.

Claims 16 and 17 recite the features that the bioartificial tissue is heart tissue having cardiomyocytes in the matrix, or skin tissue having keratinocytes in the matrix, respectively. Since claim 25, from which claims 16 and 17 depend, is patentable, claims 16 and 17 also patentable.

#### **Other Amendments**

Claims 16 and 17 have hereby been amended to recite *bioartificial* heart tissue and *bioartificial* skin tissue, respectively, instead of “synthetic” heart or skin tissue. This amendment was undertaken in order to provide consistency between the specification and the other claims of the application, which consistently refer to the tissue as “bioartificial”, not “synthetic”. For example, see claim 25, which recites “vascularized bioartificial tissue” and the first phrase of claims 16 and 17 which also recite “vascularized bioartificial tissue”; and numerous similar references throughout the specification (e.g. page 4, lines 3 and 14).

Applicant submits that this amendment thus does not add any new data to the application, and request entry of the amendment.

#### **New Claims**

New claim 26 recites a vascularized bioartificial tissue wherein the process (for making the tissue) includes the step of providing a mechanical, nutritious or migrative stimulus to said mixture during cultivation. Support for this new claim is found in the specification, for example, on page 6 at lines 21-23, and on page 16 at lines 6-7.

New claims 27-29 recite the features of the invention in which the vessel that is inserted into the cell-matrix mixture contains 1) branches or 2) lateral openings, respectively; or 3) is inherently porous. Support for the first two embodiments of the invention are found in the specification, for example, on page 5, at lines 21-22. Support for the third embodiment is found in the specification, for example, on page 5 at line 25.

In view of the support in the specification, Applicant submits that new claims 26-29 do not constitute the introduction of new matter. Applicant requests examination and allowance of new claims 26-29.


**Conclusion**

In view of the foregoing, it is requested that the application be reconsidered, that claims 14-17 and 25-29 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: ruth@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



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